

144. (Amended) The method of claim 139, wherein the photoinitiator is any dye that absorbs light having a frequency between 320 nm and 900 nm, can form free radicals, is at least partially water soluble, and is non-toxic to the at least one islet cell at the concentration used for polymerization.

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145. (Amended) The method of claim 139, wherein the macromer solution further comprises a primary, secondary, tertiary, or quaternary amine cocatalyst and the photoinitiator is selected from the group of ethyl eosin, eosin Y, fluorescein, 2, 2-dimethoxy, 2-phenylacetophenone, 2-methyl, 2-phenylacetophenone, camphorquinone, rose bengal, methylene blue, erythrosin, phloxime, thionine, riboflavin, and methyl green.

146. (Amended) The method of claim 139, wherein the microcapsule is comprised of material selected from the group of alginate, chitosan, agarose, and gelatin.

147. (Amended) The method of claim 139, wherein the macromer solution further comprises an accelerator to increase the rate of polymerization.

REMARKS

Claims 1, 130-133, and 139-147 have been amended. Claims 1 and 129-147 are now pending in this application. Amendments have been made to clarify the claimed subject matter. Accordingly, the amendments do not constitute the addition of new matter. Applicant respectfully requests the entry of the amendments and reconsideration of the application in view of the amendments and the following remarks.

The specific changes to the amended claims are shown on a separate set of pages attached hereto and entitled VERSION WITH MARKINGS TO SHOW CHANGES MADE, which follows the signature page of this Amendment. On this set of pages, insertions are underlined and deletions are bracketed.

Drawings

The Examiner has objected to the drawings as Figures 2b, 4, 6, 7a, 7b, 11b, 12a, 12b and 13 are unclear and unacceptable for printing. Applicants submit herewith the best available drawings for the above-referenced application. It is noted that Figures 2b, 4, 6, 7a, 7b, 11b, 12a,

12b and 13 are black and white photos. The original photos and negatives are no longer available.

In view of the above, withdrawal of this objection is respectfully requested.

Rejection under 35 U.S.C. § 112, first paragraph

Claims 139-147 are rejected under 35 U.S.C. § 112, first paragraph, because the Examiner asserts that the specification, while being enabled for a method comprising microencapsulating a biological material and then coating the microencapsulated material with a photoinitiator, does not reasonably provide enablement for a method of coating an islet cell with photoinitiator.

In response to this ground of rejection, Applicants have amended claim 139 to clarify that the encapsulated islet cell is coated with a photoinitiator.

In view of Applicants' amendments, this ground of rejection may be properly withdrawn.

Rejection under 35 U.S.C. § 112, second paragraph

Claims 1 and 129-147 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The Examiner asserts that the claims do not clearly recite that the islet cell is encapsulated in a microcapsule before creating a mix of islet cell, aqueous macromer solution and photoinitiator (claim 1) or before coating the islet with a photoinitiator (claim 139).

This ground of rejection is believed to be obviated by Applicants' amendment of claims 1 and 139 as kindly suggested by the Examiner. Withdrawal of this ground of rejection is respectfully requested.

Rejection under 35 U.S.C. § 102/103

Claims 1 and 129-138 are rejected under 35 U.S.C. § 102(e) as being anticipated by Soon-Shiong et al. (5,700,848 or 5,705,270 or 5,846,530).

Claims 1, 129-135 and 137-138 are rejected under 35 U.S.C. § 102(e) as anticipated by Soon-Shiong et al. (5,545,423, or 5,759,578 or 5,788,988 or 5,879,709).

In response to the above grounds of rejection, Applicants submit a copy of the Declaration under 37 C.F.R. § 1.131 that was submitted in the parent application no. 08/783,387, now U.S. Patent No. 6,258,870 (Declaration). The present application is a continuation of 08/783,387. Although the Declaration was originally submitted for the related parent application, Applicants submit that the Declaration establishes invention of the subject matter of the rejected claims prior to the effective date of the cited references.

The Rule 131 Declaration states that before Soon-Shiong '848 was filed, that is, before October 29, 1991, the co-inventors (Hubbel, Pathak, Sawhney and Desai) reduced to practice in the United States "a method of microencapsulating biological materials which comprise mixing the biological material with an aqueous macromer solution and a photoinitiator, generating microcapsules and polymerizing the gel using a light source" (Declaration, paragraph 4). Regarding the formation of small globular geometric shapes recited in claim 1 hereof, paragraph 7 of the Declaration states that the solution polymerizes into beads. Beads are a globular geometric shape. The Declaration which is supported by attached Exhibit 1, describes encapsulation of beta cells of the insuloma line.

In paragraph 10, the Declaration states that the Examiner has also cited U.S. Patent No. 5,545,423 which has a later filing date (November 25, 1991) than Soon-Shiong '848 and that consequently, the invention as claimed was also completed before this date.

As noted in the response to the Office Action in the parent application, Neil Desai refused to sign the Rule 131 Declaration because Applicants had refused to disclose confidential materials from the application to VivoRx. In this regard, a copy of the Declaration of Carol Schneider is also resubmitted.

In view of the above, withdrawal of the above grounds of rejection is respectfully requested.

Double patenting

Claims 1 and 129-147 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-69 of U.S. Patent No. 5,529,914.

Claims 1 and 129-147 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-58 of U.S. Patent No. 6,258,870.

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Claims 1 and 129-147 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-16 of U.S. Patent No. 5,858,746.

Claims 1 and 129-147 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-21 of U.S. Patent No. 5,801,033.

Claims 139-147 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-16 of U.S. Patent No. 5,843,743.

The above grounds of rejection under the judicially created doctrine of obviousness-type double patenting are believed to be obviated by Applicants' terminal disclaimer submitted herewith.

CONCLUSION

In view of Applicants' amendments to the claims and the foregoing Remarks, it is respectfully submitted that the present application is in condition for allowance. Should the Examiner have any remaining concerns which might prevent the prompt allowance of the application, the Examiner is respectfully invited to contact the undersigned at the telephone number appearing below.

Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 11-1410.

Respectfully submitted,

KNOBBE, MARTENS, OLSON & BEAR, LLP

Dated: April 14, 2003

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

Claims 1, 130-133 and 139-147 have been amended as shown.

1. (Twice Amended) A method of encapsulation of at least one islet cell encapsulated in a microcapsule, comprising the steps of:

- a) creating a mix of the at least one islet cell, [which is first]encapsulated in a microcapsule, in an aqueous macromer solution comprising macromer and photoinitiator;
- b) forming small globular geometric shapes of the mix; and
- c) polymerizing the macromer by exposing the geometric shapes to light radiation.

130. (Amended) The method of claim [2]129, wherein the macromer is selected from the group consisting of ethylenically unsaturated derivatives of poly(ethylene oxide) (PEO), poly(ethylene glycol) (PEG), poly(vinyl alcohol) (PVA), poly(vinylpyrrolidone) (PVP), poly(ethyloxazoline) (PEOX), poly(amino acids), polysaccharides, and proteins.

131. (Amended) The method of claim [3]130, wherein the [PEG]macromer is PEG tetraacrylate.

132. (Amended) The method of claim [3]130, wherein the polysaccharides are selected from the group consisting of alginate, hyaluronic acid, chondroitin sulfate, dextran, dextran sulfate, heparin, heparin sulfate, heparan sulfate, chitosan, gellan gum, xanthan gum, guar gum, water soluble cellulose derivatives and carrageenan.

133. (Amended) The method of claim [3]130, wherein the proteins are selected from the group consisting of gelatin, collagen, and albumin.

139. (Amended) A method for encapsulation of at least one islet cell[, which is first encapsulated in a microcapsule] , comprising the steps of:

- a) coating at least one islet cell encapsulated in a microcapsule with photoinitiator;
- b) suspending the at least one coated islet cell encapsulated in a microcapsule in a macromer solution comprised of macromer; and

c) irradiating the suspension with light.

140. (Amended) The method of claim [12]139, wherein the macromer is a water soluble, ethylenically unsaturated, polymer susceptible to polymerization into water insoluble polymer through interaction of at least two carbon-carbon double bonds.

141. (Amended) The method of claim [13]140, wherein the macromer is selected from the group consisting of ethylenically unsaturated derivatives of poly(ethylene oxide) (PEO), poly(ethylene glycol) (PEG), poly(vinyl alcohol) (PVA), poly(vinylpyrrolidone) (PVP), poly(ethyloxazoline) (PEOX), poly(amino acids), polysaccharides, and proteins.

142. (Amended) The method of claim [14]141, wherein the polysaccharides are selected from the group consisting of alginate, hyaluronic acid, chondroitin sulfate, dextran, dextran sulfate, heparin, heparin sulfate, heparan sulfate, chitosan, gellan gum, xanthan gum, guar gum, water soluble cellulose derivatives and carrageenan.

143. (Amended) The method of claim [14]141, wherein the proteins are selected from the group consisting of gelatin, collagen, and albumin.

144. (Amended) The method of claim [12]139, wherein the photoinitiator is any dye that absorbs light having a frequency between 320 nm and 900 nm, can form free radicals, is at least partially water soluble, and is non-toxic to the at least one islet cell at the concentration used for polymerization.

145. (Amended) The method of claim [12]139, wherein the macromer solution further comprises a primary, secondary, tertiary, or quaternary amine cocatalyst and the photoinitiator is selected from the group of ethyl eosin, eosin Y, fluorescein, 2, 2-dimethoxy, 2-phenylacetophenone, 2-methyl, 2-phenylacetophenone, camphorquinone, rose bengal, methylene blue, erythrosin, phloxime, thionine, riboflavin, and methyl green.

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146. (Amended) The method of claim [12]139, wherein the microcapsule is comprised of material selected from the group of alginate, chitosan, agarose, and gelatin.

147. (Amended) The method of claim [12]139, wherein the macromer solution further comprises an accelerator to increase the rate of polymerization.

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